ventilation (as in case 2) would have been detrimental to any patient with traumatic brain damage regardless of their Hb genotype. Giving general anaesthesia for an elective procedure in a patient with unexplained preoperative pyrexia (as in case 5) would be considered to be questionable anaesthetic practice, particularly in a patient with SS disease. The remaining deaths could not be attributed to anaesthesia or its management but rather to the poor physical condition of patients at the time of surgery, which is often associated with a high incidence of complications even in the absence of Hb S.[13]

Without physiological monitoring at the capillary level no anaesthetic can be claimed to be truly uneventful, but in this series there was no evidence to suggest that "clinically uneventful" anaesthesia provoked fatal or even serious manifestations of sickle-cell disease. Indeed, two prospective studies have shown that the number of circulating sickled cells is not increased and may actually be decreased during general anaesthesia and for some time postoperatively.[14 15] Furthermore, even major surgery could be accomplished at steady-state Hb concentrations without harm to the patient. Anaesthetic management following the important recommendations of Oduro and Searle[16] and using selective blood transfusion seems appropriate for patients with sickle-cell disease. More complex methods of management based on theoretical considerations do not appear to offer any proved advantages and may not be practical where the disease is most prevalent.

We should like to acknowledge the help of Professor S E H Brooks, head of the department of pathology, University Hospital of the West Indies, in interpreting the histological and necropsy material.

References

1 Shapiro, N D, and Poe, M F, *Anesthesiology*, 1955, **16**, 771.
2 Browne, R A, *British Journal of Anaesthesia*, 1965, **37**, 181.
3 Howells, T H, *et al*, *British Journal of Anaesthesia*, 1972, **44**, 975.
4 Rosenbaum, J M, *et al*, *Archives of Otolaryngology*, 1965, **82**, 307.
5 Rockoff, A S, *et al*, *Pediatrics*, 1978, **61**, 73.
6 Serjeant, G R, *Clinical Features of Sickle Cell Disease*. Amsterdam, North Holland, 1974.
7 American Society of Anesthesiologist, *Anesthesiology*, 1963, **24**, 111.
8 Golding, J S R, *Annals of the Royal College of Surgeons of England*, 1956, **19**, 296.
9 Thorburn, M J, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1969, **63**, 102.
10 Atlas, A S, *Journal of the American Medical Association*, 1974, **229**, 1078.
11 Spiegelman, A, *Archives of Surgery*, 1972, **104**, 761.
12 Bentley, P G, and Howard, E R, *Annals of the Royal College of Surgeons of England*, 1979, **61**, 55.
13 Keats, A S, *Anesthesiology*, 1978, **49**, 233.
14 Oduntan, S A, and Isaacs, W A, *British Journal of Anaesthesia*, 1971, **43**, 1159.
15 Maduska, A L, *et al*, *Anesthesia and Analgesia, Current Researches*, 1975, **54**, 361.
16 Oduro, K A, and Searle, J F, *British Medical Journal*, 1972, **4**, 596.

(*Accepted 18 April 1979*)

Whooping cough after stopping pertussis immunisation

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British Medical Journal, 1979, **1**, 1601-1603

Summary and conclusions

An epidemic of whooping cough occurred in a rural practice in Shetland, containing 144 children under 16. Before July 1974 all children were immunised against pertussis, but after that date immunisation was stopped. Of the 134 children studied, 93 had been immunised. Sixty-five of the children developed whooping cough. The incidence of infection was similar in those who had and had not been immunised. The incidence was also similar in those born before and after July 1974.

There was no evidence to support the routine use of pertussis immunisation in rural Shetland.

Introduction

Routine immunisation against pertussis in my Shetland practice was discontinued in July 1974. I therefore viewed the advent of the British epidemic of whooping cough in the autumn of 1977 with apprehension. In the practice no child aged under 3 years 3 months had been immunised against pertussis, whereas nearly all children over that age had been immunised in infancy. In these circumstances I considered the whooping cough outbreak to be worth study and report my findings.

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The practice

The practice covers about 50 square miles (130 sq km) of the west mainland of Shetland and the three off-shore islands of Foula, Vaila, and Papa Stour. It contains the villages of Walls and Sandness, but the population is widely scattered and the practice entirely rural. Agriculture and fishing are the main industries, and most of the patients are in social classes I, II, or III. At the time of the epidemic the practice covered 721 patients, of whom 144 were children under 16 years. There are four primary schools in the practice. From the age of 12 the children attend secondary schools outside the practice area.

Method of study

The immunisation state of the children was determined from their medical records. Whooping cough was defined as an illness characterised by a cough lasting at least four weeks associated with either whooping or vomiting.[1] In each case the date of onset and the course of the disease were recorded. The parents of all children who did not present to the doctor with whooping cough were contacted to determine whether their children had developed the disease.

Since there is no bacteriology laboratory in Shetland, the specimens have to travel by road and air to Aberdeen City Hospital. Throat swabs for routine bacteriology were taken from all the infants and from many of the older children. In 10 of the infants throat swabs were also placed in transport medium and sent for virology. In these infants pernasal swabs were also taken. These were plated out in Bordet-Gengou medium and incubated at 37°C overnight before transport to Aberdeen.

The epidemic

Table I shows the pertussis immunisation state of the children in the practice. Ten children born after July 1974 are not included,

TABLE I—*Immunisation state of children aged 0-15 years*

	Immunised	Not immunised	Total
Children born before July 1974	93	6	99
Children born after July 1974		35	35
Total	93 (69·4%)	41 (30·6%)	134*

*Ten children whose immunisation state was unknown were omitted.

either because their immunisation state was unknown (eight) or because immunisation had been only partial (two). Of the remaining 134 children, 93 (69%) had been immunised. None of those born after July 1974 had been immunised. The immunisation rate for those born before July 1974 was 94·0%. There had been no whooping cough in the practice for 15 years before the 1977 outbreak.

The first child affected in the outbreak developed symptoms of whooping cough on 2 October 1977. She was a 15-year old girl who lived four miles (6 km) from Walls and attended a school outside the practice area. She had been immunised against pertussis. Her 8-year-old sister developed the disease 10 days later. By the end of October six further children from neighbouring crofts were affected. All of these first eight cases had received pertussis immunisation.

The illness spread rapidly during November and continued into January 1978. Sixty-five (45%) of the 144 children under 16 developed whooping cough. Eight adults also sought medical help because they had whooping cough, the oldest being 69. Probably more adults were affected, but no attempt was made to trace these. The immunisation of the adults was not known and they are not included in the analysis.

Table II gives the numbers of new cases occurring in successive two-week periods of the outbreak and their immunisation state. By the end of the sixth week 24 patients had the disease, of whom 22 (92%) had been fully immunised. Table III gives the incidence of whooping cough in children born before July 1974, when an immunisation programme was in force, and in children born later, after the programme had been discontinued. Forty-nine (45%) of the

TABLE II—*Numbers of new cases of whooping cough occurring during fortnightly periods from 2 October 1977*

	Fortnightly period after 2 October 1977						
	1st	2nd	3rd	4th	5th	6th	7th
Immunised children	2	6	14	12	8	2	2
Non-immunised children			2	5	5	3	3

TABLE III—*Incidence of whooping cough in children born before and after immunisation was stopped in July 1974*

	No contracting whooping cough		
	Yes	No	Total
Children born before July 1974	49 (49*)	60	109
Children born after July 1974	16	19	35
Total	65	79	144

*Expected numbers, null hypothesis.

109 children born before July 1974 developed the disease; 16 (46%) of the 35 children born after July 1974 were affected. Whooping cough occurred in 46 (49%) of 93 immunised children and in 18 (44%) of 41 children who had not been immunised. Eight children are excluded because their immunisation state was not known, and two are excluded because immunisation was only partial.

The outbreak never reached the off-shore islands in the practice. Table IV gives the incidences of whooping cough in the immunised and non-immunised mainland children. Whooping cough occurred in 46 (54%) of the 85 fully immunised children and in 18 (56%) of the 32 children who had not been immunised. The difference is not significant. The 32 non-immunised mainland children were studied for known contact with the disease (table V). Such contacts were present in nine of the 18 children with whooping cough but in only two of those who did not develop whooping cough.

As expected, the disease was most severe in the youngest children.

TABLE IV—*Incidence of whooping cough in immunised and non-immunised children*

	No contracting whooping cough		
	Yes	No	Total
Immunised children	46 (46*)	39	85
Non-immunised children	18	14	32
Total	64	53	117

*Expected number (null hypothesis)

TABLE V—*Number of known contacts of 32 children living on mainland who had not been immunised*

	With whooping cough	Without whooping cough
No of children	18	14
No at school	2	2
No with affected sibling	7	
Total No with known contact	9	2

Three infants (aged 5 months, 6 months, and 6 months) had apnoeic attacks severe enough to cause concern, but none required hospital admission. All infants and some of the older children were treated with erythromycin or co-trimoxazole. By definition the cough always lasted at least four weeks, and many children were still coughing four months later. Chest *x*-ray films of 11 patients with persistent cough were all normal. No child suffered detectable permanent damage from the illness.

The bacteriological swabs grew *Bordetella pertussis* in only two cases, presumably because of the 48-hour transit time of specimens to the laboratory. *Streptococcus pyogenes* or *Staphylococcus pyogenes*, or both, were isolated from eight cases. From one child both *B pertussis* and *Staph pyogenes* were cultured. No viruses were isolated.

Discussion

Successive reports by the Joint Committee on Vaccination and Immunisation[2 3] have recommended routine immunisation against pertussis. Nevertheless, the value and safety of immunisation remain controversial.[4] The nationwide whooping-cough epidemic of 1977-8 afforded an opportunity for further study of the effects of immunisation. In an account of the outbreak in a practice of about 11 000 in semi-rural England Jenkinson[5] reported that the vaccine gave considerable protection, especially to infants.

I have described a whooping-cough outbreak in a small practice (just over 700) in rural Shetland. The advantages of the small rural practice in the study of infectious disease were shown nearly 40 years ago by Pickles.[6] The spread of the infection may be followed from patient to patient and from household to household. It is possible to determine positively which patients did not develop the disease as well as those who did. Large-scale studies of whooping-cough epidemics depend on notifications of disease. This is almost certainly a source of considerable error. The small size of my practice enabled me to study all children under 16 years, including those who did not present to me with the disease. Thus the figures presented, though small, are accurate.

The most interesting feature of the study was that the outbreak started and spread among the older children. The immunisation rate in this group was 94%. If the immunisation had been effective this high rate should have produced herd immunity sufficient to have prevented an epidemic. Instead almost half the children under 16 years of age and some adults were affected.

There was no significant difference in the proportion of children developing whooping cough between those born at a time when routine immunisation was given and those born after

immunisation had been discontinued (table III). Nor was there a significant difference in the incidence of whooping cough between the immunised and non-immunised children (table IV), even when the isolated children were excluded. Tables III and IV, of course, mainly compare younger children with older ones. It has been suggested that the effect of pertussis immunisation decreases with time. This effect was not apparent in this study. In fact, in the 3½- to 5-year-old age group six of the seven immunised children developed whooping cough, compared with 46 of the 85 immunised children as a whole.

Since none of the children under 3 years 3 months had been immunised, this study gives no information about the possible benefits of immunisation in this group. Jenkinson[5] reported an incidence of whooping cough in immunised children of only 5·7%. Possibly some of the 16 affected infants in my study would have been protected by immunisation. None of the three seriously ill infants, however, was over 6 months of age. Immunisation starting at this age would therefore hardly have benefited them. They might have received good protection from immunisation starting at 4 months, which is now recommended in Scotland. The infants received no apparent protection from the immunisation of their older siblings, who spread the epidemic via the schools and preschool playgroup.

The whooping-cough outbreak confirms the relative mildness of the illness now, at least in a rural community composed chiefly of people in social classes I to III. The disease was unpleasant and prolonged and caused concern to both doctor and parents, but no child needed hospital admission, and apparently none suffered permanent damage.

Benefits of immunisation must be measured against deleterious effects of the procedure. In my study one child started having convulsions on the night of his second triple inoculation in 1969 and required antiepileptic treatment until 1976. He developed whooping cough in the 1977 outbreak.

The results of this small study in a rural practice can be used only in conjunction with those elsewhere to assess the value of pertussis immunisation in the country as a whole. The newer vaccines may be more effective in producing herd immunity in the child population. My findings, however, do not support the routine use of pertussis immunisation in rural Shetland today.

I thank Dr Janet Ditchburn, who collected much of the data, and Professor Gordon Stewart, of the department of community medicine, University of Glasgow, for encouragement and the statistical analysis.

References

1 Miller, F J W, *et al*, *Growing up in Newcastle upon Tyne*, p 74. London, Oxford University Press, 1960.
2 Joint Committee on Vaccination and Immunisation of the Central Health Services Council and the Scottish Health Service Planning Council. *British Medical Journal*, 1975, **3**, 687.
3 Joint Committee on Vaccination and Immunisation, *Review of Evidence on Whooping Cough Vaccination*. London, HMSO, 1977.
4 Stewart, G T, *Lancet*, 1977, **1**, 234.
5 Jenkinson, D, *British Medical Journal*, 1978, **2**, 577.
6 Pickles, W N, *Epidemiology in Country Practice*. Bristol, Wright, 1939.

(*Accepted 4 April 1979*)

SHORT REPORTS

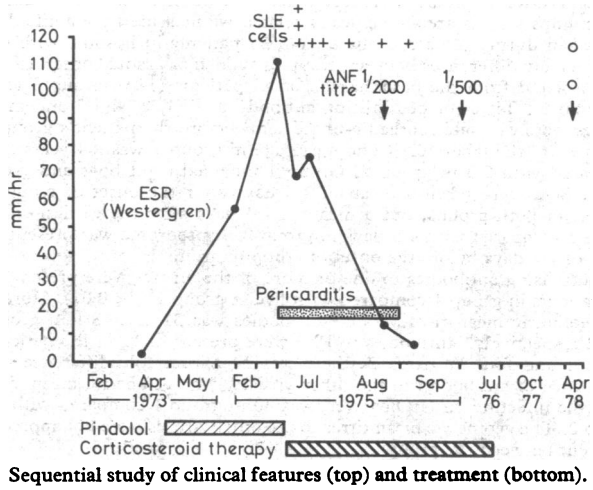
Systemic lupus erythematosus syndrome induced by pindolol

Several drugs, particularly hydrallazine and procainamide, may induce an illness resembling idiopathic systemic lupus erythematosus (SLE). Adrenergic beta-blocking agents have also been implicated since the first report by Raftery and Denman[1] concerning practolol and one possible case reported by Harrison *et al*[2] concerning propranolol. We report the case of a patient who developed an SLE syndrome while being treated with pindolol.

Case report

A 63-year-old man affected by pneumoconiosis had an inferolateral myocardial infarction in February 1973. He was treated with heparin and fluorophenylindanedione. In April 1973 he was admitted to hospital with severe angina. Pindolol 5 mg three times a day by mouth was added to his treatment. His clinical course (figure) was uneventful until February 1975, when he was thought to have a postmyocardial infarction shoulder-hand syndrome and was treated with phenylbutazone. At the end of June 1975 he was readmitted with fever (38·5°C), severe chest pain, and complaining of symmetrical polyarticular arthralgias affecting mainly the fingers, hands, shoulders, wrists, and, to a lesser extent, the knees and ankles. Values for serum enzymes were within normal limits. The red blood cell count was $3{\cdot}9 \times 10^{12}$/l (3 900 000/mm³), the white blood cell count $3{\cdot}2 \times 10^{9}$/l (3200/mm³), and ESR (Westergren) 112 mm in the first hour. Blood concentration of urea nitrogen was 14·5 mmol/l (40·6 mg/100 ml) (normal 2·5-6·5 mmol/l (7-18 mg/100 ml)) and serum creatinine concentration 141 μmol/l (1·5 mg/100 ml) (normal 80-115 μmol/l (0·9-1·3 mg/100 ml)). There was neither proteinuria nor haematuria. At the beginning of July 1975 a loud pericardial friction rub was heard and the ECG showed widespread T-wave inversion. Chest *x*-ray examination showed changes suggestive of pericardial effusion. Systemic lupus erythematosus was suspected. This was confirmed by the presence of large numbers of lupus erythematosus (LE) cells in the blood, while the latex test for rheumatoid factor was negative.

A diagnosis of drug-induced SLE seemed probable. Among the drugs taken by the patient pindolol appeared most likely to be responsible. It was stopped. Methylprednisolone 80 mg was given intravenously daily. In August 1975 bilateral pleural effusions appeared. Large numbers of LE cells continued to be found in the blood and the test for antinuclear antibody detectable by immunofluorescence was positive at a titre of 1/2000. The test for antibodies to denaturated (single-stranded) DNA detectable by the Farr technique (Peltier *et al*[3]) gave an index of 0·22. The test for antibodies to native (double-stranded) DNA gave an index of 0·04 (the test is positive when the index is more than 0·10). Methylprednisolone by mouth was continued at an initial dose of 1 mg/kg/day and then gradually reduced. The temperature fell to normal after a few days and the ESR was 14 mm in the first hour at the end of August 1975. Chest *x*-ray examination at the beginning of September showed resolution of the pleural effusions and a normal heart size. The patient was discharged in the middle of September without any symptoms. Corticosteroid treatment was continued up to July 1976. The clinical course was then uneventful up to April 1978. An immunological study at that time showed a positive response of the blastic transformation of lymphocytes in the presence of pindolol.



Sequential study of clinical features (top) and treatment (bottom).

Comment

This case may be considered as one of drug-induced SLE-like syndrome. After the withdrawal of the suspected drug the clinical